REMARKS

Courtesies extended to Applicants' representative Kenneth Jenkins during the telephone conference conducted March 27, 2009, are acknowledged with appreciation.

I. STATUS OF THE CLAIM

No claims are amended. Claims 1 to 9, 11, 12, 14 and 16 to 23 are pending.

II. REJECTION OF CLAIMS 1-9, 11, 12, 14, 16-23 UNDER 35 U.S.C. §103(a)

Claims 1-9, 11, 12, 14 and 16-23 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Alatossava *et al.* (US Pat. No. 5,849,488, hereinafter "Alatossava").

A. The Law Regarding Obviousness

The Examiner is respectfully reminded that the USPTO bears the burden of establishing a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). Only if this burden is met does the burden of coming forward with rebuttal arguments or evidence shift to the applicant. *Rijckaert*, 9 F.3d at 1532, 28 USPQ2d at 1956. When the references cited by the examiner fail to establish a *prima facie* case of obviousness, the rejection is improper and will be overturned. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988)." *See In re Deuel*, 51 F.3d 1552, 34 USPQ2d 1210, 1214 (Fed. Cir. 1995).

In order to establish a *prima facie* case of obviousness based on a combination of elements from the cited art, one of skill must have had a reasonable expectation of successfully using the product of the suggested combination:

> The prior art can be modified or combined to reject claims as prima facie obvious as long as there is a reasonable expectation of success. In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)

See MPEP §2143.02(I). Moreover, the expectation of success required by the law must be rooted in some degree of predictability within the art:

> Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). ... See also Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1207-08, 18 USPQ2d 1016, 1022-23 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991)...; In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

See MPEP §2143.02(II). Furthermore, all claim limitations must be considered:

> 'All words in a claim must be considered in judging the patentability of that claim against the prior art.' In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

See MPEP §2143.03. Finally, omission of an element with retention of the function of the element indicates unobviousness:

> Note that the omission of an element and retention of its function is an indicia of unobviousness. In re Edge, 359 F.2d 896, 149 USPQ 556 (CCPA 1966).

See MPEP §2144.04(II)(B).

B. A Prima Facie Case of Obviousness Has Not Been Established with Respect To The Method of Alatossava.

As acknowledged by the Examiner, Alatossava does not explicitly disclose the required claim element of "contacting said crude milk sample with a fluorescent label." *See* Office Action at page 3, lines 16-18. The Examiner further accurately states that "Alatossava et al. do not explicitly disclose using a fluorescent label DNA probe for target nucleic acid detection." *See* Office Action at page 4, lines 7-8. Thus, the present obviousness rejection rests on the assertion that it would have been obvious to apply the method of Alatossava to detect DNA by using a fluorescent label with a crude milk sample to arrive at the claimed invention. *See* Office Action at page 4, lines 9-12. Applicants respectfully disagree.

Throughout Alatossava, detection of DNA is limited to DNA which has been isolated. *See inter alia* Alatossava at Col. 4, lines 16-17, line 25, line 49; Col. 6, lines 21-24, lines 60-63; Col. 8, lines 13-15. Isolated DNA, as disclosed by Alatossava, is not DNA in a crude milk sample as contemplated in the current claims. For example, Alatossava discloses that detection of a PCR-amplified target sequence in a milk sample is achieved through gel electrophoresis or using double-stranded (ds)-DNA specific stains or antibodies, conducted after the PCR reaction:

> In summary, for the purpose of a mastitis diagnosis both the infection study and the inflammation study can be performed by PCR with specific primer pairs simultaneously after DNA from the mastitis milk sample has been isolated using relatively simple and rapid procedures as shown in examples 6 and 7. The time required for isolating DNA from a milk sample for PCR reactions was less than 130 min. The DNA amplification step took about 110 min with a conventional PCR device (example 2), but only 20 min with an ATC-type PCR device (example 3). An analysis of PCR products with agarose gel electrophoresis (with 150 V voltage in 1.5% agarose in 1.times. TBE buffer) in the presence of ethidium bromide could be performed in 15 min. It is also possible to use alternative systems to measure (semi)quantitatively the amounts of ds-DNA after PCR reactions e.g. fluorometrically or immunologically using ds-DNA specific stain or antibodies, respectively.

See Alatossava at Col. 6, line 58 to Col. 7, line 7. Gel electrophoresis is a method for isolating DNA. Thus, after reading Alatossava, one of ordinary skill in the art would recognize a need to isolate DNA prior to quantitative, or even semi-quantitative, detection. Accordingly, Alatossova provides no reasonable expectation of success for detecting DNA in a crude milk sample in which the DNA has not been isolated, as currently claimed. *See* MPEP §2143.02(I).

Alatossava further discloses the detection of DNA target sequences in milk by hybridization. If hybridization is used for the detection of target sequences in milk, Alatossava teaches that the target sequence is denatured and isolated prior to hybridization:

> The presence of the target sequences can be determined in any conventional way e.g. by hybridization or preferably by polymerase chain reaction (PCR) as previously described e.g. in Ehrmann et al., FEMS Microbiol. Lett. 117 (1994) 143-150 and

> Barry et al., PCR Methods and Applications 1 (1991) 51-56, respectively. For hybridization purposes, the isolated DNA is first denaturated and then reacted with e.g. a labeled complementary probe under conditions enabling hybridizaton, whereafter the amount of hybrid-bound probe is measured. In PCR, a primer pair is used which recognizes complementary strands of the DNA segment to be enzymatically amplified. The amplified DNA segment (usually about 0.2-2 kb) can then be detected e.g. by gel electrophoresis.

See Alatossava at Col. 4, lines 43-56. Thus, in view of Alatossava, the skilled artisan would recognize a need to isolate the target DNA prior to hybridization with a probe. Accordingly, Alatossova provides no reasonable expectation of success for detecting DNA in a crude milk sample, as currently claimed. *See* MPEP §2143.02(I).

Applicants respectfully submit that all of the various reactions involving DNA as disclosed by Alatossava require isolated DNA because crude milk samples include light scattering components which, absent their separation from the labeled DNA, would be expected to adversely affect the detection of the labeled DNA. The light scattering component include, for example, milk proteins, lipoproteins, fat globules, micelles and the like, all of which generally scatter light. Based on the knowledge of these scattering problems, Alatossava uses amplification and/or purification steps to successfully detect target sequences in milk samples, thereby avoiding light scattering problems. Accordingly, the skilled artisan reading Alatossava would have no reasonable expectation of successfully implementing fluorescence-based detection of DNA in a crude milk sample because scattered light would be considered to directly affect the detection of fluorescence. *See* MPEP §2143.02(II).

In contrast, the present claims are directed to methods and kits which contemplate detection of a fluorescent label in crude milk samples. Indeed, Applicants were the first to discover a method of successfully detecting DNA in crude milk samples using fluorescent labels without resorting to DNA isolation. The present claims omit the steps of purification and amplification as taught by Alatossava and still successfully detect the target sequence in a crude milk sample. Thus, it was discovered that omission of DNA isolation in a crude milk sample

resulted in retention of the ability to quantitate the DNA, which is indicative of unobviousness. *See* MPEP §2144.04(II)(B).

Furthermore, Applicants respectfully submit that the Examiner may not permissibly ignore the term "crude milk sample" contained within independent claims 1, 12 and 22. The term "crude milk sample" refers to a raw sample from which the milk fat has not been removed. *See* for example paragraph [0029]. Thus, the term "crude milk sample" excludes the DNA isolation disclosed by Alatossava, but the law requires that all of the words in a claim must be considered in judging the patentability of that claim against the prior art. *See* MPEP §2143.03. Thus, the current claims are not obvious over Alatossava.

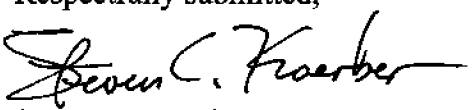
In conclusion, Applicants respectfully submit that a *prima facie* case for obviousness has not been set forth because one of skill would not have had any reasonable expectation of successfully or predictably removing the isolation steps set forth in the method of Alatossava to arrive at Applicants' claimed method including "detecting said fluorescent label in said crude milk sample." Accordingly, Applicants respectfully request withdrawal of the current rejection and allowance of the pending claims.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. An action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6100.

Respectfully submitted,



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